510(k) Summary

Applicant:

Quidel Corporation
10165 McKellar Court
San Diego, California 92121
Telephone: 858-552-7910
Fax: 858-646-8045

Contact Information:

Ronald H. Lollar, Senior Director Clinical and Quality Affairs
1055 East State Street
Suite 100
Athens, Ohio 45701
740-589-3300 – Corporate number
740-589-3373 – Desk phone
740-593-8437 – Fax
lollar@dhiusa.com

Date of preparation of 510(k) summary:

November 30, 2011

Device Name:

Trade name – **Quidel Molecular hMPV Assay**
Classification name – Respiratory viral panel multiplex nucleic acid assay
Product Code – OEM
Regulation – 21 CFR 866.3980

Legally marketed devices to which equivalence is claimed:

Gen-Probe Prodesse Pro hMPV+ (k082688)

The Pro hMPV+ Assay is a Real Time RT-PCR *in vitro* diagnostic test for the qualitative detection of human Metapneumovirus (hMPV) nucleic acid isolated and purified from nasopharyngeal swab (NP) specimens obtained from individuals exhibiting signs and symptoms of acute respiratory infection. This assay targets a highly conserved region of the Nucleocapsid gene of hMPV. The detection of hMPV nucleic acid from symptomatic patients aids in the diagnosis of human respiratory hMPV infection if used in conjunction with other clinical and laboratory findings. This test is not intended to differentiate the four genetic sub-lineages of hMPV.

Negative results do not preclude hMPV infection and should not be used as the sole basis for diagnosis, treatment or other management decisions.

Intended Use:

The Quidel Molecular hMPV assay is a multiplex Real Time RT-PCR assay for the *in vitro* qualitative detection of human metapneumovirus RNA in nasal and nasopharyngeal swab specimens from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of human metapneumovirus infections in humans in conjunction with clinical and epidemiological risk factors. This test is not intended to differentiate the four genetic sub-lineages of hMPV.

Negative results do not preclude hMPV infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

Device Description:

The Quidel Molecular hMPV Assay detects viral nucleic acids that have been extracted from a patient sample using the NucliSENS® easyMAG® automated extraction platform. A multiplex RT-PCR reaction is carried out under optimized conditions in a single tube generating amplicons for each of the target viruses present in the sample. This reaction is performed utilizing the Applied Biosystems® 7500 Fast Dx platform. Identification of hMPV occurs by the use of target specific primers and a fluorescent- labeled probe that hybridizes to conserved regions in the RNA dependent RNA polymerase gene of hMPV.

The following is a summary of the procedure:

1. **Sample Collection:** Obtain nasal or nasopharyngeal swab specimens using standard techniques from symptomatic patients. These specimens are transported, stored, and processed according to established laboratory procedures.

2. **Nucleic Acid Extraction:** Extract Nucleic Acids from the specimens with the NucliSENS easyMAG System following the manufacturer's instructions using the appropriate reagents.

   Prior to the extraction procedure add 20 µL of the Process Control (PRC) to each 180 µL aliquot of specimen. The PRC serves to monitor inhibitors in the extracted specimen, assures that adequate amplification has taken place and that nucleic acid extraction was sufficient.

3. **Rehydration of Master Mix:** Rehydrate the lyophilized Master Mix using 135µL of Rehydration Solution. The Master Mix contains oligonucleotide primers, fluorophore and quencher-labeled probes targeting highly conserved regions of hMPV as well as the process control sequence. The primers are

complementary to highly specific and conserved regions in the genome of the virus. The probes are dual labeled with a reporter dye attached to the 5'end and a quencher attached to the 3' end. The rehydrated Master Mix is sufficient for eight reactions.

4. **Nucleic Acid Amplification and Detection: Add** 15 µL of the rehydrated Master Mix to each reaction plate well. 5µL of extracted nucleic acids (specimen with PRC) is then added to the plate well. Then place the plate into the Applied Biosystems 7500 FastDx.

   Once the plate is added to the instrument, the assay protocol is initiated. This protocol initiates reverse transcription of the RNA targets generating complementary DNA, and the subsequent amplification of the target amplicons occurs. The Quidel Molecular hMPV assay is based on TaqMan® chemistry, and uses an enzyme with reverse transcriptase, DNA polymerase, and 5'-3' exonuclease activities. During DNA amplification, this enzyme cleaves the probe bound to the complementary DNA sequence, separating the quencher dye from the reporter dye. This step generates an increase in fluorescent signal upon excitation by a light source of the appropriate wavelength. With each cycle, additional dye molecules are separated from their quenchers resulting in additional signal. If sufficient fluorescence is achieved by 35 cycles during the data collection stage of amplification, the sample is reported as positive for the detected nucleic acid.

Device Comparison

The Quidel Molecular hMPV assay was compared to legally marketed RT-PCR assay. The characteristics of Quidel Molecular hMPV assay ("Subject Device") and the Prodesse Pro hMPV+ ("Predicate Device") are described in Table 5.1, below:

Table 5.1:	**Subject Device and Comparator Device Comparison**	
Item	**Subject Device** Quidel Molecular hMPV Assay	**Predicate Device** Prodesse ProFlu+
Intended Use	The Quidel Molecular hMPV assay is a multiplex Real Time RT-PCR assay for the in vitro qualitative detection of human metapneumovirus RNA in nasal and nasopharyngeal swab specimens from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of human metapneumovirus infections in humans in conjunction with clinical and epidemiological risk factors. This test is not intended to differentiate the four genetic sub-lineages of hMPV. Negative results do not preclude hMPV infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.	The Pro hMPV+ Assay is a Real Time RT-PCR *in vitro* diagnostic test for the qualitative detection of human Metapneumovirus (hMPV) nucleic acid isolated and purified from nasopharyngeal swab (NP) specimens obtained from individuals exhibiting signs and symptoms of acute respiratory infection. This assay targets a highly conserved region of the Nucleocapsid gene of hMPV. The detection of hMPV nucleic acid from symptomatic patients aids in the diagnosis of human respiratory hMPV infection if used in conjunction with other clinical and laboratory findings. This test is not intended to differentiate the four genetic sub-lineages of hMPV. Negative results do not preclude hMPV infection and should not be used as the sole basis for diagnosis, treatment or other management decisions.
Assay Target	hMPV	hMPV
Sample Types	nasal and nasopharyngeal swab specimens	nasopharyngeal swab
Extraction Methods	bioMérieux easyMAG Automated Magnetic Extraction Reagents	Roche MagNA Pure LC Total Nucleic Acid Isolation Kit or the bioMérieux easyMAG Automated Magnetic Extraction Reagents
Assay Methodology	PCR-based system for detecting the presence or absence of viral RNA in clinical specimens	PCR-based system for detecting the presence or absence of viral RNA in clinical specimens
Detection Techniques	Multiplex assay using different reporter dyes for each target	Multiplex assay using different reporter dyes for each target

Table 5.1:	**Subject Device and Comparator Device Comparison**	
Item	**Subject Device** Quidel Molecular hMPV Assay	**Predicate Device** Prodesse ProFlu+
Viral Targets	RNA polymerase gene	Nucleocapsid
LoD	The analytical sensitivity (limit of detection or LoD) of the Quidel Molecular hMPV assay was determined using quantified ($TCID_{50}$/mL) cultures of 4 hMPV strains (A1, A2, B1, B2) serially diluted in negative nasopharyngeal matrix. Each dilution was extracted using the NucliSENS easyMAG System and tested in replicates of 20 per concentration of virus on both the Applied Biosystems® 7500 Fast Dx platform. Analytical sensitivity (LoD) is defined as the lowest concentration at which 95% of all replicates tested positive, ranged from 10^1 to 10^0 $TCID_{50}$/mL.	The analytical sensitivity (limit of detection or LoD) of the Pro hMPV+ Assay was determined using quantified (TCID50/mL) cultures of 2 hMPV (subtype A2 and subtype B2) strains serially diluted in nasopharyngeal clinical matrix. Each viral strain was extracted using the Roche MagNA Pure LC instrument and tested in replicates of 20 per concentration of virus. Analytical sensitivity (LoD) as defined as the lowest concentration at which ≥ 95% of all replicates tested positive, ranged from 10^2 – 10^1 $TCID_{50}$/mL.

Analytical Performance:

Reproducibility:

The reproducibility of the Quidel Molecular hMPV assay was evaluated at 3 laboratory sites. Reproducibility was assessed using a panel of 4 simulated samples that included a medium positive hMPV sample (2.65E+02 $TCID_{50}$/mL), a low positive hMPV sample (1.06E+02 $TCID_{50}$/mL), a high negative hMPV sample (1.59E+01 $TCID_{50}$/mL) and a negative. Panels and controls were tested at each site by 2 operators for 5 days in triplicate (2 operators X 5 days X triplicate testing X 3 sites = 90 results per sample). The panels and controls were extracted using the bioMérieux easyMAG system and tested on the ABI 7500Fast Dx.

Table 5.2: Reproducibility										
Panel Member ID	**Site 1**			**Site 2**			**Site 3**			**Total Results**
	Results	**AVE Ct**	**%CV**	**Results**	**AVE Ct**	**%CV**	**Results**	**AVE Ct**	**%CV**	
hMPV High Negative (1.59E+01 $TCID_{50}$/mL)	10/30	33.36*	5.08	10/30	32.76*	3.38	0/30	N/A	N/A	20/90
hMPV Low Positive (1.06E+02 $TCID_{50}$/mL)	30/30	28.73	5.28	30/30	28.18	8.42	29/30	30.18	4.89	89/90
hMPV Medium Positive (2.65E+02 $TCID_{50}$/mL)	30/30	25.09	6.65	30/30	25.18	7.63	30/30	26.58	5.68	90/90
Negative Sample	0/30	N/A	N/A	0/30	N/A	N/A	0/30	N/A	N/A	0/30
hMPV Positive Control	30/30	18.37	3.88	30/30	18.48	4.35	30/30	18.60	3.08	90/90
Negative Control	0/30	N/A	N/A	0/30	N/A	N/A	0/30	N/A	N/A	0/30

* CV of positive results

The data from the combined sites indicates that the Quidel Molecular hMPV assay generates reproducible results for hMPV when tested with the ABI 7500 Fast Dx.

Limit of Detection

The analytical sensitivity (limit of detection or LoD) of the Quidel Molecular hMPV assay was determined using quantified ($TCID_{50}$/mL) cultures of 4 hMPV strains (A1, A2, B1, B2) serially diluted in negative nasopharyngeal matrix. Each dilution was extracted using the NucliSENS easyMAG System and tested in replicates of 20 per concentration of virus on both the Applied Biosystems® 7500 Fast Dx platform. Analytical sensitivity (LoD) is defined as the lowest concentration at which 95% of all replicates tested positive.

Table 5.3: Level of Detection	
Strain	**Final $TCID_{50}$/mL LoD 7500 Fast Dx**
hMPV A1	5.29E+01
hMPV A2	1.39E+01
hMPV B1	3.15E+00
hMPV B2	1.07E+01

Analytical reactivity (inclusivity)

The reactivity of the Quidel Molecular hMPV assay was evaluated against multiple strains of hMPV. The clinical panel consisted of 12 hMPV strains (3 A-1, 2 A-2, 3 B-1, and 4 B-2). Each panel member was extracted using the NucliSens easyMAG instrument and tested in triplicate.

The Quidel Molecular hMPV assay detected 100% of the hMPV at 10^0 to 10^2 $TCID_{50}$/mL levels on both the Applied Biosystems® 7500 Fast Dx platform.

Table 5.4: hMPV Inclusivity Panel

Subtype	Strain	$TCID_{50}$/mL	(7500 Dx)
A1	Italy	1.11E+2	Positive
B1	Italy	2.20E+0	Positive
B2	Italy	4.50E+1	Positive
B1	Peru2-2002 G Gene	4.17E+2	Positive
B2	Peru1-2002 G Gene	1.26E+2	Positive
B1	Peru3-2003 G Gene	1.26E+2	Positive
B2	Peru6-2003	5.01E+2	Positive
A1	IA3-2002 G Gene	1.51E+2	Positive
A1	IA10-2003	3.80E+2	Positive
B2	IA18-2003 G Gene	6.61E+2	Positive
A2	IA14-2003 G Gene	1.95E+2	Positive
A2	Clinical Isolate	1.05E+2	Positive

Analytical specificity (cross-reactivity)

The analytical specificity of the Quidel Molecular hMPV assay was evaluated by testing a panel consisting of 26 viral, 24 bacterial, and 1 yeast strain representing common respiratory pathogens or flora commonly present in nasopharynx. Bacteria and yeast were tested at concentrations of 10^5 to 10^{10} CFU/mL. Viruses were tested at concentrations of 10^3 to 10^8 $TCID_{50}$/mL. Samples were extracted using the NucliSENS easyMAG instrument and tested in triplicate. Analytical specificity of the Quidel Molecular hMPV assay was 100%.

Table 5.5: Cross-reactivity

Organism ID	TCID50/mL or CFU/mL	hMPV Result

Table 5.5: Cross-reactivity

Organism ID	TCID50/mL or CFU/mL	hMPV Result
RSV Long	4.40E+04	Negative
RSV Washington	1.75E+04	Negative
A/Mexico/4108/2009	1.40E+07	Negative
B/Florida/04/2006	5.25E+05	Negative
Adenovirus 1/Adenoid 71	5.67E+04	Negative
Coronavirus 229E	1.70E+06	Negative
Coronavirus OC43	1.67E+06	Negative
Coxsackievirus B4	2.43E+06	Negative
Coxsackievirus B5/10/2006	2.28E+06	Negative
Cytomegalovirus	8.76E+05	Negative
Echovirus 7	5.38E+08	Negative
Echovirus 9	1.50E+06	Negative
Echovirus 6	1.05E+08	Negative
Echovirus 11	1.50E+05	Negative
Enterovirus 71	2.68E+03	Negative
Enterovirus 70	1.66E+05	Negative
Epstein Barr Virus	5,000cp/mL	Negative
HSV Type 1 MacInytre strain	1.95E+06	Negative
HSV Type 2 G strain	3.67E+06	Negative
Rubeola	3.78E+05	Negative
Mumps virus	8.43E+04	Negative
Parainfluenza Type 1	2.50E+05	Negative
Parainfluenza Type 2	2.20E+04	Negative
Parainfluenza Type 3	9.10E+05	Negative
Parainfluenza Type 4	9.57E+06	Negative
Varicella Zoster Virus	7.50E+02	Negative
Bordetella pertussis	1.04E+07	Negative
Bordetella bronchiseptica	2.55E+07	Negative
Chlamydia trachomatis	2.10E+05	Negative
Legionella pneumophila	2.05E+08	Negative
Mycobacterium intracellulare	6.90E+08	Negative
Mycobacterium tuberculosis	6.60E+07	Negative
Mycobacterium avium	1.36E+10	Negative
Haemophilus influenzae	5.90E+07	Negative
Pseudomonas aeruginosa	5.15E+07	Negative

Table 5.5: Cross-reactivity		
Organism ID	**TCID50/mL or CFU/mL**	**hMPV Result**
Proteus vulgaris	2.65E+08	Negative
Proteus mirabilis	2.75E+07	Negative
Neisseria gonorrhoeae	2.15E+07	Negative
Neisseria menigitidis	1.85E+08	Negative
Neisseria mucosa	1.85E+08	Negative
Klebsiella pneumoniae	3.30E+07	Negative
Escherichia coli	6.80E+07	Negative
Moraxella catarrhalis	5.85E+07	Negative
Corynebacterium diptheriae	6.0E+05	Negative
Lactobacillus plantarum	1.03E+08	Negative
Streptococcus pneumoniae	4.5E+07	Negative
Streptococcus pyogenes	2.05E+08	Negative
Streptococcus salivarius	2.50E+06	Negative
Staphylococcus epidermidis	2.6E+07	Negative
Staphylococcus aureus	5.15E+08	Negative
Candida albicans	1.07E+06	Negative

Clinical Performance:

Performance characteristics of the Quidel Molecular hMPV assay were established during a prospective study during the 2010-2011 respiratory virus season (January to March 2011). A total of 1116 specimens were evaluated in this study (742-fresh, 374-frozen). Of the fresh specimens, 399 specimens were nasal swabs, and 343 were nasopharyngeal swabs. The fresh specimens were collected for routine respiratory virus testing at thirteen sites across the United States. The frozen specimens were collected and tested at two geographically distinct locations and were comprised of 374 nasopharyngeal swabs.

The 1116 specimens were tested by both the subject and a comparator device for human metapneumovirus RNA. Sixteen of these specimens were invalid on initial testing with the subject device (1.4%). Re-testing of the specimens according to the Interpretation algorithm described above also yielded invalid results. Thirty-six specimens were invalid on initial and repeat testing (as per the device's package insert) on the comparator device (3.2%). The invalid specimens have been removed from the additional analysis. The Table 5.6 below details the results for the remaining 1072 specimens.

Table 5.6: Clinical Performance Data			
Nasal/nasopharyngeal swab (N=1072)	**FDA Cleared RT-PCR**		
Quidel Molecular	Positive	Negative	Total
Positive	60	2*	62
Negative	3	1007	1010
Total	63	1009	1072
			95% CI
Positive Percent Agreement	60/63	95.2%	86.7 to 99.0%
Negative Percent Agreement	1007/1009	99.8%	99.3% to 100%

* Specimens negative for hMPV by sequence analysis

Conclusions

Quidel Molecular hMPV Assay yielded good positive and negative percent agreement for nasal and nasopharyngeal swabs when compared to a 510(k) cleared molecular device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Quidel Corporation
c/o Ronald H. Lollar
Senior Director, Clinical and Quality Affairs
1055 East State Street
Suite 100
Athens, Ohio 45701

DEC 15 2011

Re: K112490
Trade/Device Name: Quidel Molecular hMPV Assay
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OEM
Dated: November 18, 2011
Received: November 21, 2011

Dear Mr. Lollar:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use Statement

510(k) Number (if known): k112490

Device Name: Quidel Molecular hMPV Assay

Indication for Use:

The Quidel Molecular hMPV assay is a multiplex Real Time RT-PCR assay for the *in vitro* qualitative detection of human metapneumovirus RNA in nasal and nasopharyngeal swab specimens from patients with signs and symptoms of respiratory infection. This test is intended for use as an aid in the differential diagnosis of human metapneumovirus infections in humans in conjunction with clinical and epidemiological risk factors. This test is not intended to differentiate the four genetic sub-lineages of hMPV.

Negative results do not preclude hMPV infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

Prescription Use		Over-The-Counter Use
X	AND/OR	
(Part 21 CFR 801 Subpart D)		(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic
Device Evaluation and Safety

510(k) K112490